HISTORY

146 Excessive Bleeding and Bruising

R. L. PALMER

Definition

The spectrum of the clinical entity ranges from pinpoint cutaneous hemorrhage (petechiae) covering the lower extremities to a catastrophic fulminant and often fatal form associated with internal bleeding. The clinician should be alert that a hemostatic problem possibly exists when undue bleeding is observed that is inconsistent with antecedent trauma, occurs from two or more anatomic sites, or lasts for over 24 hours.

Technique

The physician is usually confronted with two questions: What clinical and historical features suggest abnormal bleeding, and what is the link, if any, between comorbid conditions or medications? This chapter does not discuss disorders causing local injury to vasculature such as peptic ulcer or cancer but concentrates on systemic processes affecting hemostasis.

A well-taken history supplies important clues in identifying bleeding disorders. The object is to find useful points that predict those patients who truly have a problem. Even patients in whom the coagulation tests show nothing at all should be viewed with proper suspicion when significant historic features are discovered. The problem of normal coagulation tests in the face of bleeding is discussed under Clinical Significance. Potential useful information may be a family history of bleeding, comorbid disease, medications, the pattern (petechiae, ecchymosis, etc.) and duration of bleeding, and the circumstances affecting bleeding.

The patient should be questioned about spontaneous nosebleeds and bruises, menstrual blood flow longer than 5 days, and bleeding for over 36 hours' duration after dental extraction. Spontaneous bruising is important, but the bruise should be over 3 cm in size to be significant and no aspirin taken during the prior week. Fair, fat females will often unknowingly bump objects and develop small, innocent bruises, usually on the proximal extremities. It is important to ask about blood transfusion requirements for any type of surgery, especially minor surgery.

Extravasation of blood into soft tissues after trauma should be ascertained by asking the patient or family whether big blue areas of swelling have occurred on the neck, buttocks, or about the joints. It is virtually impossible for an active youngster to have a significant bleeding problem and not experience large hematomas, synovial bleeding, or bleeding into musculature. A bleeding disorder beginning after the age of 20 suggests an acquired hemostatic defect, while symptoms beginning in childhood suggest a congenital disorder.

A careful drug history is mandatory. Many medications affect the platelet count but do not affect the coagulation proteins unless liver damage has occurred or the patient is surreptitiously taking coumadin or heparin. The clinician should narrow his sights to simplify the questions an I ask specifically about aspirin products (over-the-counter products such as Alka-Seltzer) and nonsteroidal anti-inflammatory agents (NSAIAs) if the platelet count is normal.

A wide variety of drugs may lower the platelet count; medication can either suppress bone marrow production of platelets or increase the rate of peripheral platelet destruction. Drug-induced suppression may occur at the bone marrow stem cell level affecting all of the cellular elements of the blood (pancytopenia), the most notable drugs being the cancer chemotherapeutic agents. When decreased platelet survival is present, an isolated low platelet count is found. Medications such as quinidine or ones containing a sulfonaminide chemical structure are often the causative agents, but more than 50 drugs have been reported. Frequently, the patient will have comorbid diseases that may produce a low platelet count (e.g., infection, liver disease, or autoimmune disease) so that timely observation may be required to exclude the medication being the cause. Thrombocytopenia usually resolves within 2 weeks following discontinuation of the offending agent, but much more slowly if bone marrow hypocellularity exists, and sometimes not at all.

One of the arts practiced by the experienced physician is drawing sufficient conclusions from insufficient premises. The type of bleeding provides further evidence of predictive value for diagnosis. Useful points are as follows:

1. Petechiae are attributable to platelet or vascular abnormalities; if systemic symptoms are present and the petechiae are tender and elevated, vasculitis should be suspected.
2. Large subcutaneous ecchymoses (bruises) without petechiae suggest coagulation factor deficiencies from liver disease or von Willebrand's disease.
3. Hemarthroses usually indicate one of the hemophilias (factor VIII, IX, or XI deficiency).
4. Purpura (intracutaneous bleeding) may be associated with petechiae or ecchymoses and can have allergic connotations, such as immune complexes that damage the capillary endothelium. These processes may occur up to 6 weeks after an infection and can present as an explosive onset of purpura and gastrointestinal bleeding.
5. Telangiectasias, when they occur on the lips or mucous membranes, herald potential hemoptysis, hematemesis, hematuria, or melena.
6. Hospitalized patients who start to ooze blood around catheters and blood-letting sites should alert the physician to check for disseminated intravascular coagulation, vitamin K deficiency, or thrombocytopenia.

The above-mentioned events should serve as guides for formulating a rational plan for diagnostic studies.

Basic Science

Traditional medicine has centered on the concept that either coagulation protein or blood vessel wall and platelet aggregation abnormalities are the etiologies for venous and arterial bleeding. While true in most cases, these concepts may be challenged as too simplistic to account for all the complex bleeding problems that may occur. It should be clear that the hemostatic mechanism that involves interrelated biologic and physiologic systems by which blood remains fluid or gels may be altered in many ways. There is no common denominator among the various elements (the vascular endothelium, blood platelets, soluble coagulation proteins, plasmin, and the intrinsic anticoagulation system) that contribute to clotting. One or more may be altered quantifiably or qualitatively. So, too, active bleeding may use up coagulation proteins so that sharp separation between the original or inciting abnormality and later acquired deficiencies may be difficult to sort out. One is often left with attempting to develop a temporal relationship between the disease state and the interpretation of abnormal coagulation tests obtained later.

As a result of vessel wall injury, two processes are initiated that play important roles in thrombus formation. Platelets attach to subendothelial collagen; adenosine diphosphate (ADP) is released from their dense bodies, organelles residing in the platelet's cytoplasm. While this process is occurring, arachidonic acid is being converted by a series of enzymatic reactions to thromboxane A_2 via the prostaglandin pathway. The rate-limiting enzyme in this reaction is cyclooxygenase, the enzyme inhibited by aspirin and the NSAIAs. Thromboxane A_2 potentiates the aggregating capability of ADP and is itself a potent vasoconstrictor. Platelet aggregation may occur independent of thromboxane A_2, which provides a reason for the lack of the protective effect of aspirin in many patients suffering from thrombo-occlusive disease.

Another mechanism considered to be important in the platelet interaction with the subendothelium is von Willebrand factor, which we might term platelet Super Glue. Von Willebrand factor (VWF) is a portion of the factor VIII molecule that allows the initial platelet plug formed at the injury site to withstand the shearing force of flowing blood. Evidence suggests the VWF activity depends on the interaction of VWF with platelet membrane protein receptor, glycoprotein I_b. Thus, patients may have hemorrhagic disorders from either reduced VWF activity or abnormalities in its platelet receptor. Another mechanism of importance later on in clotting is that of fibrinogen, which attaches to platelet membrane receptor glycoprotein II_b/III_a complex.

As all these events are occurring, there is a realignment of membrane phospholipids so that their negatively charged polar head groups are exposed to the plasmatic milieu. Thus the outside of the platelet membrane, previously composed of neutral phospholipids that have no clot-promoting ability, becomes negatively charged and effects clotting. The active platelet phospholipid surface may now be termed platelet factor III. One can see that deficiencies in ADP, in fibrinogen, in von Willebrand factor, in thromboxane A_2, or in the phospholipid reversing mechanism might inhibit platelet participation in coagulation and produce bleeding.

Once platelet factor III is activated, coagulation factors are concentrated on the platelet surface where fibrinogen is immediately available via the previously described mechanism. Two unique complexes composed of coagulation protein form on the negatively charged platelet surface: one complex contains factors VIII, IX, and X; the second, termed the prothrombinase complex, contains coagulation factors V, activated X, and prothrombin (II). Figure 146.1 demonstrates the coagulation scheme and the involvement of the various platelet mechanisms with the plasmatic coagulation factors. This simplified process does not address the question of how the extrinsic pathway enters the picture. When tissue is injured, thromboplastin is released and activates factor VII, which in turn activates factors X and IX. Therefore, the complex previously described at the platelet surface containing factors VIII, IX, and X can be activated by either factor XI or factor VII. This dual amplification system leads to a tremendous increase in the rate of thrombin formation.

Fibrinogen conversion to fibrin by thrombin is enhanced by fibrinogen binding to glycoprotein II_b/III_a at the platelet surface; consequently, a higher rate of fibrin formation is observed than if fibrinogen were floating free in the plasma. Once the fibrin net (after cross-linking of fibrin monomer by factor XIII) occurs, it reinforces the platelet aggregate at the site of injury to form a stable thrombus plug.

Clinical Significance

The etiologies of hemorrhagic disease can be categorized as follows:

- Vessel wall mediated
- Vascular endothelial injury
- Platelet deficiencies
- Coagulation protein deficiencies
- Antithrombotic agent usage
- Natural anticoagulant pathway disorders
- Disseminated intravascular coagulation (DIC) and/or fibrinolysis

VESSEL WALL MEDIATED

Surgical management of vascular injuries and slippage of ligatures are not discussed. Recognition of local causes should be in the forefront of any investigatory effort when bleeding occurs in the nose, lungs, gastrointestinal or genitourinary tracts, and central nervous system, or when rebleeding occurs in the postoperative patient.

Senile, glucocorticoid, or fragile skin purpura is a very common and distinct entity that may frighten the patient when large 1 to 5 cm in diameter irregular lesions with clear-cut margins arise on the extensor surfaces of the forearm and hand, thus distinguishing them from ecchymoses in which the margins are poorly defined. The patient should be reassured that no systemic bleeding is associated, since there is no generalized increase in capillary fragility.

Five types of telangiectasia are recognized, two of which are of clinical importance in hemostasis. Unlike petechiae, all five types of lesions will blanch when pressed upon by a glass slide. Significant hemorrhage does not occur from simple telangiectasia on the skin of the face, senile ectasia or cherry angiomas usually found on the trunk, or spider angiomas or pulsating telangiectasia found on the upper portions of the body. Hereditary hemorrhagic telangiectasia (HHT) is a hereditary dominant trait in which the outstanding features may be small dilated capillaries on the lips, nasal mucosa membranes, tongue, face, and hands in descending frequency. The skin lesions may be varied and inconspicuous, but profuse internal hemorrhage may occur. The hemorrhagic tendency increases with age and is possibly related

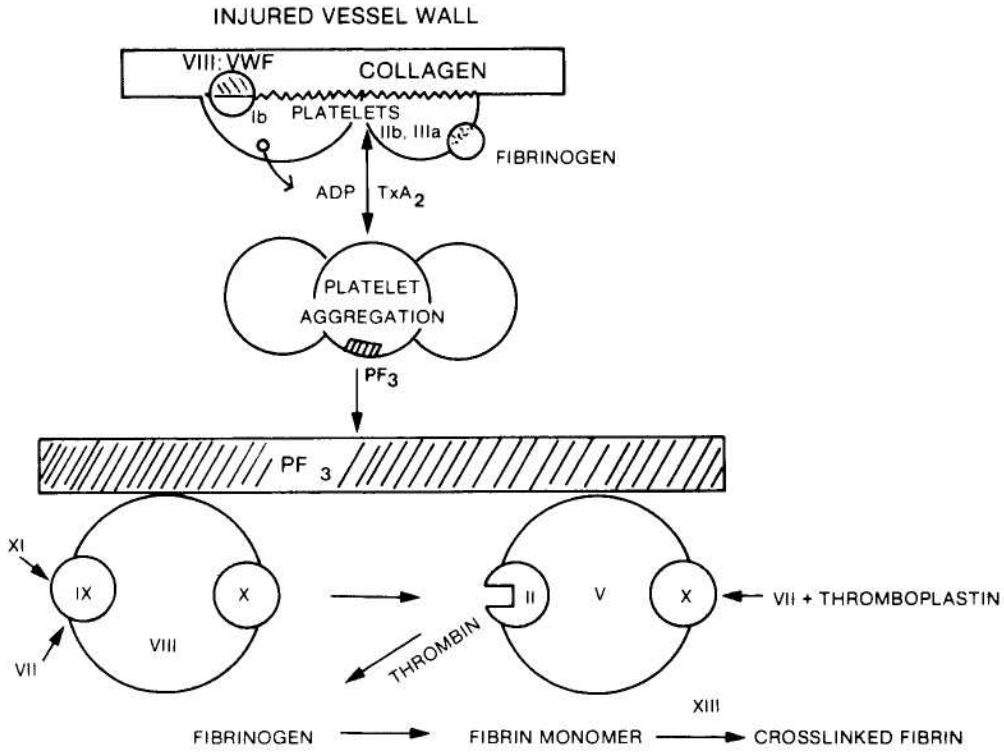

Figure 146.1
Pathway of Hemostasis
VIII:VWF = von Willebrand factor
I_b = Glycoprotein I_b VWF platelet receptor complex.
II_b, III_a = Glycoprotein platelet fibrinogen receptor complex
ADP = Adenosine diphosphate
TxA_2 = Thromboxane A_2
II = Prothrombin
PF_3 = Negatively charged platelet phospholipid surface

to senile perivascular tissue atrophy or heightened fibrinolytic activity due to increased concentrations of tissue plasminogen activator. The second disorder that may lead to bleeding is that of acquired dilation of bowel capillaries (angiodysplasia). These lesions vary from the size of a pinhead to that of a pea and occur in the ascending colon of the elderly and may produce significant gastrointestinal bleeding. Skin manifestations are lacking, and diagnoses may be difficult. All tests of hemostasis are normal in angiodysplasia and HHT.

VASCULAR ENDOTHELIAL INJURY

These vascular disorders are a heterogeneous group that usually cause bleeding in the form of petechiae and small ecchymosis, although fulminating hemorrhages may occur. Systemic infections, drugs, and poorly understood immunologic factors may be the etiology. An infection may precede bleeding from days to weeks. Coagulation studies are normal. Rarely, the capillary fragility test and the Simplate bleeding time are abnormal. A variety of antigen–antibody reactions are capable of producing hemorrhage whether directly attacking the vascular endothelium or lodging on the endothelium as an innocent bystander. The most frequently encountered is in small vessels. Necrosis involves the entire wall with accumulation of granulocytes; many organs may be involved including the brain, heart, kidney, and lungs. Immune complex may fix complement to the cell surface, increase vascular permeability, and cause tissue necrosis resulting in a systemic necrotizing vasculitis or present as the Henoch–Schonlein syndrome. In many instances the offending antigen is unknown. Additionally, many agents (virus, rickettsiae, drugs, etc.) may directly injure vascular endothelium.

PLATELET DEFICIENCIES

Broadly speaking, if there is no evidences of other cytopenias in the face of a low platelet count, the cause is either medication, platelet antibodies, hypersplenism, infection, or a bone marrow production defect. Methods for measuring platelet antibodies are not within the capability of most laboratories, so other tests should be performed to exclude the aforementioned disorders. These tests would include an antinuclear antibody test of lupus erythematosus, a direct Coombs test for antibodies on red cells, and a bone marrow aspiration and biopsy for myelophthisic processes. Timely observation after omission of medications has been previously described.

When the platelet count is normal but the patient has a qualitative platelet defect with an abnormal Simplate bleeding time, the most likely causes are medication, the myeloproliferative disorders, chronic renal failure, or an inherited platelet function defect. Further tests, which include platelet aggregation studies, are necessary to define acquired or inherited platelet function defects.

COAGULATION PROTEIN DEFICIENCIES

The hemorrhagic disorders, von Willebrand's disease (VWD), and hemophilia A are most frequently encountered inherited coagulation factor deficiencies. In order to understand and manage these disorders, it is mandatory to have some knowledge of the macromolecular structure of the factor VIII complex, which is a multimer of a basic molecule. Most agree that the basic molecule can be regarded as having two subunits: one is of lower molecular weight and contains factor VIII coagulant activity (VIII:C); the other is of higher molecular weight and contains factor VIII, von Willebrand factor (VIII:VWF), and VIII:VWF antigen (protein). It may be seen that varying quantities or activities of these two subfractions can be present, thereby causing variabilities in the hemostatic test results that check VIII:C and VIII:VWF. In most laboratories these tests are the activated partial thromboplastin time (aPTT) for VIII:C and the Simplate bleeding time for VIII:VWF. The major problem that complicates the diagnosis of VWF is that the levels of VIII:C and VIII:VWF may not be reduced in activity enough to produce the classic pattern of laboratory abnormalities such as an abnormal PTT and bleeding time. Hence, other solutions are needed to diagnose the variant forms of VWD. Von Willebrand factor causes the aggregation of platelets in vitro when ristocetin is added. In the absence of von Willebrand factor, ristocetin will not induce platelet aggregation. So, too, if the larger subunits of the factor VIII molecule containing VIII:VWF are reduced, then the antigen level of this subfraction is reduced. Measurements of ristocetin aggregation and VIII von Willebrand factor antigen levels are helpful in sorting out the various forms of VWF and may be required for diagnosis. This is of extreme importance because one of the pitfalls that the clinician must avoid in VWF is to be fooled into thinking that he is dealing with a qualitative or functional platelet defect in a patient who has epistaxis and purpura when only the bleeding time is abnormal. Platelet transfusion will not correct the problem. Von Willebrand's disease should be treated by transfusion of factor VIII cryoprecipitate to correct a qualitative deficiency or by infusing desmopressin acetate for a quantitative deficiency.

Hemophilia A is not as complex an issue, since the problem is reduced activity of VIII:C only. The bleeding problems are usually more severe than VWD, and platelet deficiency bleeding (e.g., petechiae and epistaxis) is not seen. Bleeding occurs in males who are hemizygous for the abnormal X chromosome transmitted by a heterozygous mother who is an asymptomatic carrier. Body parts subject to injury (such as joints and muscles) are involved by hemarthrosis or deep hematomas. Surrounding tissue damage may be severe due to diminished blood flow from the tamponade effect of large hematomas. The level of VIII:C varies from individual to individual, so bleeding can be serious when VIII:C activity is less than 1% or quite mild when greater than 5%. Like VWD, bleeding episodes are treated by transfusion of factor VIII cryoprecipitate. For major surgery or after trauma, the level of factor VIII should be maintained above 50% of normal for several days. Management problems arise in 10 to 20% of patients who produce antibodies after repeated transfusions against factor VIII. Several therapeutic approaches are tried: factor IX complex transfusion to bypass the factor VIII defect; desmopressin acetate infusion to mobilize endogenous factor VIII; plasmapheresis to remove antibody; and immunosuppressant therapy to suppress antibody formation.

Factor IX deficiency is also transmitted as an X-linked recessive trait like factor VIII; factor IX deficiency is transmitted as an autosomal recessive trait. Although quite rare, factor XI deficiency may be seen in both males and females; bleeding may be mild and, unlike VIII and IX deficiency, may begin with the gastrointestinal tract. Inherited factor VIII and factor IX deficiencies are not found in females unless there is a history of consanguinity in the family or it is due to an acquired inhibitor in a previously healthy individual.

Inhibitors, which are antibodies to any of the coagulation proteins, may form for unknown reasons and appear spontaneously. They may disappear just as quickly if the patient is not rechallenged by some exogenous or unknown antigen. More common antibodies are for factors II, V, VIII, or X. These may develop in patients with various diseases and usually cause minor bleeding. Examples are antibodies for factors II and VIII in autoimmune disease, X in primary amyloidosis, and V after blood transfusion.

Chronic liver disease can result in multiple bleeding problems. The use of factor IX concentrate (which contains factors II, VII, IX, and X) is of benefit, but is limited by its thrombogenicity and a significant rate of hepatitis infection. Fresh frozen plasma may be used for the patient with end-stage liver disease or for any patient who does not require large amounts of a deficient coagulation factor and can thus tolerate the significant plasma volume expansion that is produced by transfusion of 1000 to 2000 ml of fresh frozen plasma.

ANTITHROMBOTIC AGENT USAGE

Thrombocytopenia complicating heparin therapy has been reported to occur due either to heparin-induced antibody damage of platelets or to poorly understood increased platelet aggregability. The platelet count should be monitored during heparin therapy.

When a patient is started on warfarin, the physician should be aware that several commonly used medications potentiate its action. Common examples are NSAIAs, tolbutamide, cimetidine, and quinidine preparations. The list is continuously revised and should be reviewed from time to time. Also, the use of antibiotics for a concurrent illness may increase the prothrombin time due to reduced vitamin K absorption from the bowel.

NATURAL ANTICOAGULANT PATHWAY DISORDERS

The clinical manifestations of deficiencies of these factors have only recently been recognized. Ordinarily, hypercoagulability occurs in the form of deep venous thrombosis or arterial thrombo-occlusive disease, but bleeding may also occur. This system holds clotting in check so that some feeble stimulus does not trigger the cascade to produce disseminated clotting even in healthy persons. The most important natural anticoagulants are antithrombin III and protein C. Antithrombin III, or heparin cofactor, neutralizes thrombin and factor X and other activated clotting factors; protein C neutralizes factors V and VIII. Considerable data support the existence of inhibitors of protein C and antithrombin III. The importance of abnormalities of these substances awaits further study, but excessive activity may occur in some diseases, leading to bleeding. The full impact on our understanding of unusual bleeding and clotting problems is yet to be determined. Additionally, stimuli that induce the release of tissue plasminogen activator from vascular endothelium (thereby producing local fibrinolysis of

a growing clot) may promote bleeding. Several possibilities therefore exist in this pathway and may lead to bleeding. These include increased cofactor reactivity such as protein S interacting with protein C, decreased inhibitor activity of one of the naturally occurring anticoagulants, or variable sensitivity of these proteins to as yet undefined activators and inhibitors.

DISSEMINATED INTRAVASCULAR COAGULATION (DIC)

Researchers have tried for many years to find easily measurable factors that would predict a hypercoagulable state that would lead to DIC; so far, efforts have failed except when deficiencies exist in the naturally occurring anticoagulation pathway previously mentioned. DIC is usually a diffuse clotting phenomenon within the microcirculation; it occurs as a sequela of a primary disease. Although usually diffuse, local bleeding or single organ damage may occur and obscure the picture. The kidney is particularly vulnerable to damage. A milder form of chronic DIC may exist secondary to malignancy or other chronic disease. The clinical presentation can be confusing, diverse, and difficult to diagnose. The warning signs may be the previously mentioned oozing of blood around indwelling catheters or generalized petechiae and purpura. Thrombocytopenia may be the first sign of DIC; platelets may be quickly consumed and serious bleeding occur. As the process continues, various coagulation proteins are used up, fibrin (fibrinogen) degradation products are released by the action of plasmin on fibrin and act as anticoagulants, and kidney, heart, or central nervous system damage can overshadow the clinical picture. Three pathophysiologic forms are recognized:

1. Clotting with secondary fibrinolysis. The primary stimulus is released thromboplastic substances from various tissue (e.g., abruptio placentae).
2. Clotting and fibrinolysis. Platelets are the primary stimulus in this form, and the consequences can be catastrophic (e.g., meningococcemia).
3. Fibrinolysis. A rare form when found alone due to plasmin activation causing fibrinogen consumption (e.g., cancer of the prostate).

The first step in management is to identify and modify the underlying cause if possible. Replacement therapy using coagulation factor concentrates and platelets should be administered; heparin therapy is considered only if vasoocclusive disease is causing the majority of the patient's morbidity.

Special Recognition and Treatment Problems

When commonly used tests of hemostasis (platelet count, Simplate bleeding time, partial thromboplastin time, prothrombin time, and thrombin time) are normal or borderline in the face of bleeding or in a preoperative patient who has a suspicious history, the physician is understandably perplexed. First, some knowledge of a differential diagnosis is needed so that alternative diagnostic studies can be utilized when available. Second, if the patient should bleed, a therapeutic strategy is needed even if the diagnosis is unclear.

Table 146.1 provides guidelines for diagnosis of the problem patient. For better understanding, it is necessary to know about the limitations of traditional coagulation studies. These studies are global in their assessment and are based on the detection of a blood clot in a test tube. Several factors are checked at one time; 30% activity of the factor is all that is needed to normalize the test. Disorders that may escape detection are mild cases of coagulation factor deficiency in which factor levels may fluctuate enough to normalize the test, von Willebrand's disease, platelet function defects, factor XIII deficiency, and as yet poorly understood abnormalities of the naturally occurring anticoagulant pathway. These disorders may require special tests that are unavailable in many hospital laboratories or tests so rarely performed that results are questionable.

Replacement Therapy

If platelet numbers and function are normal but the patient has major bleeding due to an unknown coagulation factor deficiency, certain general therapeutic principles may be followed; these also apply to known coagulation disorders.

Table 146.1
Interpretation of Laboratory Tests of Hemostatic Function

Laboratory test					
BT	PC	aPTT	PT	TT	Usual diagnosis
A	A	N	N	N	Immunothrombocytopenia or primary marrow disorder
A	N	N	N	N	Platelet function defect or von Willebrand's disease
A	N	A	N	N	von Willebrand's disease
N	N	A	N	N	Hemophiliac states
N	N	A	A	N	Abnormal vitamin K dependent coagulation factors or liver disease
A	A	A	A	A	Late disseminated intravascular coagulation, end-stage liver disease, or heparin administration
N	N	N	N	N	Borderline coagulation factor decrease, vascular bleeding, platelet function defect, or factor XIII deficiency

Source: Palmer RL. Laboratory diagnosis of bleeding disorders. Postgrad Med 1984;76:137–148.
A, abnormal; N, normal.
Tests: aPTT, activated partial thromboplastin time; BT, bleeding time; PC, platelet count; PT, prothrombin time; TT, thrombin time.

Table 146.2
Replacement Therapy[a]

Preparation	Cost ($)	Volume (dl)	Coagulation units per unit volume	Comment
Fresh frozen plasma	20	230	200	All factors present
Factor VIII cryoprecipitate	20	20	100	Single donor. Contains 250 mg fibrinogen
Factor VIII	40	20	250	Pooled plasma.
Lyophilyzed	70	40	500	Viral hepatitis and AIDS
Cryoprecipitate	130	40	1000	transmission
Factors II, VII, IX, and X complex	80	20	450[b]	Thrombogenic. Pooled plasma
Platelets	20	40	0	± 5000 mm^3 increase in recipient's platelet count

[a]Values are approximations and may vary slightly.
[b]Prothrombin complex lists variable content of factor IX only. Factors II, VII, and X units may be lower and are not given for each batch.

The deficient factor or factors should be given in sufficient amounts to assure temporary hemostasis. The frequency of administration depends on four points: the extent of trauma and potential for repeat bleeding; the type of surgery or anatomic area of the injury (head and retropharyngeal versus less potentially dangerous areas); the metabolic half-life of the deficient factor, if known; and the risk of circulatory system overload. Table 146.2 supplies important information regarding available replacement therapies. Concentrates prepared from pooled human plasma may transmit either viral hepatitis or acquired immunodeficiency syndrome. All commercial concentrates now available in the United States are viral inactivated. This information should be considered in determining the use of concentrates extracted from pooled versus single donor human plasma.

The dose of the coagulation factor is calculated in units. About 1 unit is present in 1 ml of normal human plasma. Levels may vary somewhat, but for clinical purposes it is accurate enough. The amount needed varies and should be individualized, depending on the four points mentioned previously. Generally, if hemorrhage is severe or occurs into a potentially dangerous site, one should give the number of units normally present in the patient's plasma volume. The patient's plasma volume may be calculated based on the assumption that there is 40 ml of plasma per kilogram of body weight (example: a 50-kg patient × 40 ml equals 2000 ml plasma volume). To ensure a sufficiency dose of coagulant in an unknown coagulopathy, the equivalent of at least 50% of all the factors should be administered in the form of fresh frozen plasma (FFP). In the example given above, 1000 to 2000 ml of FFP would be given while the diagnosis is being established. Concentrates obviously are much safer to administer because of potential circulatory system overload. Replacement of 100% (2000 units) of factor VIII in the aforementioned patient if he had hemophilia A would require only 80 ml of factor VIII cryoprecipitate versus 2000 ml of FFP (see Table 146.2). Remember that repeat transfusions are necessary to compensate for factor utilization and half-life and to maintain a minimal plasma concentration in vivo of 40% of the factor.

If platelet numbers or function are felt to be the cause of hemorrhage, efforts should be made to find the reason for decreased numbers or function. Platelet transfusions may remedy the problem, but alloimmunization eventually occurs after several transfusions, reducing the yield. When platelet antibodies are present in the plasma due to idiopathic thrombocytopenic purpura or alloimmunization, the life span of the transfused platelets may be so brief that there is no benefit from a platelet transfusion.

It is anticipated that one unit of platelet concentrate will increase the platelet count by 5000/mm^3; unfortunately, this may not always be the case. Bleeding usually ceases if the platelet count is maintained above 20,000 to 30,000/mm^3, provided that normal platelet function is present.

References

Bussel BB. Circulating anticoagulants: physiologic and pathophysiologic. Hosp Pract 1983;18:169–86.
Hackett T, Kelton JG, Powers P. Drug induced platelet destruction. Semin Thromb Hemostas 1982;8:116–37.
Nydegger UE, Miescher PA. Bleeding due to vascular disorders. Semin Hematol 1980;17:178–89.
Owen WG. The control of hemostasis. Arch Pathol Lab Med 1982;106:209–13.
*Palmer RL. Laboratory diagnosis of bleeding disorders. Postgrad Med 1984;76:137–48.
Weiss JS. Congenital disorders of platelet function. Semin Hematol 1980;17:228–41.